

**DOCKET NO.: ISIC-0004.100**  
**(ISIS -4823)**

**Listing of Claims**

This listing of claims will replace all prior versions, and listings, of claims in the application:

1. (Previously presented) A delayed release oral formulation for enhanced intestinal oligonucleotide absorption, comprising:

(a) a first population of carrier particles comprising said oligonucleotide and a penetration enhancer, wherein said oligonucleotide and said penetration enhancer are released at a first location in the intestine; and

(b) a second population of carrier particles comprising a penetration enhancer and a delayed release coating or matrix, wherein said penetration enhancer is released at a second location in said intestine downstream from said first location, whereby absorption of said oligonucleotide is enhanced when said oligonucleotide reaches said second location.

2. (Canceled)

3. (Previously presented) The formulation of claim 1, wherein the oligonucleotide is an antisense oligonucleotide.

4. (Previously presented) The formulation of claim 1, wherein the penetration enhancer in (a) and (b) is the same.

5. (Previously presented) The formulation of claim 1, wherein the penetration enhancer in (a) and (b) is different.

6. (Previously presented) The formulation of claim 1, wherein the penetration enhancer is selected from the group consisting of a fatty acid, bile salt, chelating agent and non-chelating non-surfactant.

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7. (Original) The formulation of claim 6, wherein said fatty acid is selected from the group consisting of arachidonic acid, oleic acid, lauric acid, capric acid, caprylic acid, myristic acid, palmitic acid, stearic acid, linoleic acid, linolenic acid, dicaprate, tricaprate, monoolein, dilaurin, glyceryl 1-monocaprate, 1-dodecylazacycloheptan-2-one, an acylcarnitine, an acylcholine, a monoglyceride and a pharmaceutically acceptable salt thereof.

8. (Original) The formulation of claim 6, wherein said bile acid is selected from the group consisting of cholic acid, dehydrocholic acid, deoxycholic acid, glucolic acid, glycholic acid, glycodeoxycholic acid, taurocholic acid, taurodeoxycholic acid, chenodeoxycholic acid, ursodeoxycholic acid, sodium tauro-24, 25-dihydrofusidate, sodium glycodihydrofusidate, polyoxyethylene-9-lauryl ether and a pharmaceutically acceptable salt thereof.

9. (Original) The formulation of claim 6, wherein said chelating agent is selected from the group consisting of EDTA, citric acid, a salicylate, an *N*-acyl derivative of collagen, laureth-9, an *N*-amino acyl derivative of a beta-diketone and a mixture thereof.

10. (Original) The formulation of claim 6, wherein said non-chelating non-surfactant is selected from the group consisting of an unsaturated cyclic urea, 1-alkyl-alkanone, 1-alkenylazacycloalkanone, steroid anti-inflammatory agent and mixtures thereof.

11. (Original) The formulation of claim 1, wherein said formulation is a capsule, tablet, compression coated tablet or bilayer tablet.

12. (Original) The formulation of claim 1, wherein said carrier particles are bioadhesive.

13. (Previously presented) The formulation of claim 1, wherein said carrier comprises a substance selected from the group consisting of poly-amino acids, polyimines,

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polyacrylates, polyalkylacrylates, polyoxethanes, polyalkylcyanoacrylates, cationized gelatins, albumins, starches, acrylates, polyethylene glycol, DEAE-derivatized polyimines, pollulans and celluloses.

14. (Original) The formulation of claim 1, wherein said carrier particles comprise a material selected from the group consisting of chitosan, poly-L-lysine, polyhistidine, polyornithine, polyspermines, protamine, polyvinylpyridine, polythiodiethylamino-methylene P(TDAE), polyaminostyrene, poly(methylcyanoacrylate), poly(ethylcyanoacrylate), poly(butylcyanoacrylate), poly(isobutylcyanoacrylate), poly(isohexylcyanoacrylate), DEAE-methacrylate, DEAE-ethylhexylacrylate, DEAE-acrylamide, DEAE-albumin, DEAE-dextran, polymethylacrylate, polyhexylacrylate, poly(D,L-lactic acid), poly(D, L-lactic-coglycolic acid) (PLGA) and polyethylene glycol (PEG).

15. (Original) The formulation of claim 1, wherein said carrier particles are cationic.

16. (Previously presented) The formulation of claim 15, wherein said carrier particles comprise a complex of poly-L-lysine and alginate, a complex of protamine and alginate, lysine, dilysine, trilysine, calcium, glucosamine, arginine, galactosamine, nicotinamide, creatine, lysine-ethyl ester or arginine ethyl-ester.

17. (Original) The formulation of claim 1 wherein said delayed release coating or matrix is selected from the group consisting of acetate phthalate, propylene glycol, sorbitan monooleate, cellulose acetate phthalate (CAP), cellulose acetate trimellitate, hydroxypropyl methyl cellulose phthalate (HPMCP), methacrylates, chitosan, guar gum and polyethylene glycol (PEG).

18. (Previously presented) A method for enhancing the absorption of a drug in a animal, comprising administering a pharmaceutical formulation of claim 1 to said animal.

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19. (Original) The method of claim 18, wherein said animal is a mammal.

20. (Original) The method of claim 19, wherein said mammal is a human.

21. (Previously presented) The formulation of claim 3 wherein the antisense oligonucleotide comprises at least one modified sugar moiety.

22. (Previously presented) The formulation of claim 21 wherein the modified sugar moiety is a 2'-methoxyethoxy sugar moiety (2'-MOE).

23. (Previously presented) The formulation of claim 1, wherein the second population of carrier particles does not contain said oligonucleotide.